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Health related quality of life following oral cancer: 10-year outcomes

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Abstract:	Objective The aim is to report 10-year health-related quality of life (HRQOL) outcomes following the treatment of oral squamous cell carcinoma (OSCC). Study Design Cross-sectional HRQOL surveys collated over a 13-year period for patients treated from 1992 gave a cohort of 674 patients with OSCC who had undergone treatment with curative intent. HRQOL measured using the UWQOL closest to 2 and 10 years. Results UWQOL data were available for 67% (154) of 230 patients alive at 10 years. Three-quarters reported their overall QOL as good, very good or outstanding. Free-flap surgery was the strongest predictor of overall QOL being less than good at 10 years. A significant problem or dysfunction was reported by a minority of patients, ranging from 7% to 13% across the 12 UWQOL domains. At the group level the changes from 2 years to 10 years were minimal with some improvement observed in appearance, chewing, mood and anxiety and deterioration in regard to swallowing. There was considerable scatter in individual changes over time. Conclusions As a group, HRQOL at 10 years is similar to that at 2 years however at an individual patient level domains were not so stable.

Statement of Clinical Relevance (max 40 words)

Long-term HRQOL following oral cancer: 10-year outcomes are very important when reporting the results of treatment.

This is the first study to report large numbers and to be able to look specifically at difference between two years and ten years.

Health related quality of life following oral cancer: 10-year outcomes

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Key words: oral cancer; mouth neoplasm; squamous cell carcinoma, ten years; long term; health related quality of life; UW-QOL

Abstract

Objective. The aim is to report 10-year health-related quality of life (HRQOL) outcomes following the treatment of oral squamous cell carcinoma (OSCC).

Study Design. Cross-sectional HRQOL surveys collated over a 13-year period for patients treated from 1992 gave a cohort of 674 patients with OSCC who had undergone treatment with curative intent. HRQOL measured using the UWQOL closest to 2 and 10 years.

Results. UWQOL data were available for 67% (154) of 230 patients alive at 10 years. Three-quarters reported their overall QOL as good, very good or outstanding. Free-flap surgery was the strongest predictor of overall QOL being less than good at 10 years. A significant problem or dysfunction was reported by a minority of patients, ranging from 7% to 13% across the 12 UWQOL domains. At the group level the changes from 2 years to 10 years were minimal with some improvement observed in appearance, chewing, mood and anxiety and deterioration in regard to swallowing. There was considerable scatter in individual changes over time.

Conclusions As a group, HRQOL at 10 years is similar to that at 2 years however at an individual patient level domains were not so stable.

Health related quality of life (HRQOL) is a key outcome following treatment for head and neck cancer (HNC). [1] Although there are numerous publications in this field [2] there are a few papers reporting on long-term HRQOL outcomes in HNC [3-9] and even fewer reporting specifically on oral cancer. [10,11] Previous literature has tended to consider 'long-term' in terms of several earlier years following diagnosis and treatment; however, 'late-effects' has emerged as an important issue and outcomes should be considered beyond five years. The importance of long-term outcomes and survivorship is reflected in national documents and initiatives across all cancers. Also, there is appreciation of late effects and how these might impact on HRQOL. [12]

Bjordal et al [3,4] reported high levels of disease and treatment related symptoms such as dryness in the mouth and mucus production and psychological distress (30% of 'cases' according to the GHQ-20), 7 to 11 years after radiotherapy treatment for HNC. We have reported quality of life 5-10 years after primary surgery for oral and oro-pharyngeal cancer, however this study was small (48 patients) and cross-sectional. [5] The findings suggested that long-term survivors tend to report a good or excellent quality of life, with outcomes similar to those at one year. This result is at variance with Mehanna [7] as their cohort showed a deterioration in overall QOL (life satisfaction) after 10 years, though they too had a small sample size and cross-sectional design. Yan and co-workers [11] reported QOL 8-year following oral cancer, in a prospective study with 30 long-term survivors. Clinically and statistically significant improvements between diagnosis and 8 years were seen for pain, mood and anxiety, whereas problems with chewing, speech, shoulder mobility, and taste worsened.

The findings from the small number of studies so far are inconclusive and the aims of this paper are to report the health-related quality of life outcome at around 10-years and compare 10-year outcomes to those reported at two years in a larger number of oral cancer patients.

MATERIAL AND METHODS

Patients

The population comprised all patients presenting to Aintree University Hospital with oral squamous cell carcinoma (OSCC) between 1 January 1992 and 31 August 2004. Patients

treated with palliative intent, those with cognitive impairment or living overseas were excluded.

Variables and measurements

The UWQOL questionnaire is well established [2] and from 1995 we have regularly used this to survey OSCC patients at various times after primary diagnosis. The UW-QOL v4 questionnaire consists of 12 single item domains, with between 3 and 5 response options scaled evenly from 0 (worst) to 100 (best) according to response hierarchy. [13] UW-QOL domains are presented within two subscales, physical function and social-emotional, as derived from earlier work.[14] The physical function score is the mean of the appearance, swallowing, chewing, speech, taste and saliva domain scores, while the social-emotional score is the mean of the pain, activity, recreation, shoulder, mood and anxiety domain scores. Subscale scores were computed so long as there were 4 or more domain scores available and published criteria used to identify which patients have a significant problem or dysfunction.[15] There is also a single item overall QOL question on the UWQOL v4 for which patients are asked to consider not only physical and mental health, but also other factors, such as family, friends, spirituality or personal leisure activities important to their enjoyment of life.

For patients alive at 10 years their UWQOL record closest to 10 years was selected within a time window requirement of being at least 8 years on from baseline (primary surgery or diagnosis if no surgery). These records were all after year 2000 and hence UWQOL version 4. To enable a comparison of UWQOL close to 2 and 10 years for patients alive at 10 years their UWQOL record closest to 2 years was selected within a time window of 12-36 months. Many patients around 2 years responded to earlier versions of the UWQOL in which the taste, saliva, mood and anxiety domains in particular were absent.

Statistical analysis

Fishers exact test was used to test for association of baseline categories with survival at 10 years, and to overall QOL being less than good after 10 years. Responses to each UWQOL domain were summarised into three categories – dysfunction, best possible response and responses that fell between these two extremes. In regard to within-patient change data over time (2 and 10 years), the McNemar test (2 categories) or the McNemar-Bowker test (3 categories) was used to test paired table symmetry. Cohen's kappa coefficient was used to measure agreement in paired categorical data over time; values <0.20 reflect ‘poor’

agreement, 0.21-0.40 ‘fair’, 0.41-0.60 as ‘moderate’, 0.61-0.80 ‘good’ and >0.80 as ‘very good’. The Paired t- test was used to compare paired numerical UWQOL domain scores over time, and 95% confidence intervals for the mean change were computed. The Wilcoxon test was used to compare paired subscale scores.

This study was approved by Aintree University Hospital Audit Department as part of annual surveys and data collected in routine care.

RESULTS

There were 674 eligible patients and their characteristics are shown in Table 1. Overall survival at 10 years was 34% (230/674), 95% CI 30.5-37.8%. Baseline age, tumour staging, free-flap surgery and primary treatment were associated ($p<0.001$) with overall survival at 10 years (Table 1). UWQOL data closest to 10 years (and at least 8 years on) was available for 67% (154/230), at a median (IQR) of 121 (117-125) months from baseline. Free-flap surgery was the strongest predictor of overall QOL being less than good at 10 years (Table 1), 45% for patients with composite flaps, 26% with soft flaps and 14% without a free-flap. Other negative prognostic trends were observed for advanced tumours and for patients earlier in the cohort, though it was noted that the use of composite flaps fell from 25% in 1992-6 to 12% in 2002-4 and the use of any free-flap from 81% to 64%.

A significant problem or dysfunction was indicated from the responses given by a minority of patients, ranging from 7% to 13% across the 12 UWQOL domains (Table 2). Otherwise, there was a fairly even split in patient response between the best possible response (35% to 50% across domains) and being somewhere between the two extremes (33% to 54%). Overall quality of life was good or better for 74% (112/151) and the median physical function and social-emotional subscale median scores were 80 and 83 respectively (Table 3).

Tables 4 and 5 show UWQOL domain results for 113 patients with data close to 10 years (at least 8 years on) at a median (IQR) of 121 (117-124) months and close to 2 years (within 12-36 months) at a median (IQR) of 25 (20-28) months. The main observation is that changes in the UWQOL results were quite similar at 2 and 10 years in regard to the domain categorisations (Table 4) and numerical mean domain scores (Table 5). Both tables suggested small improvements in appearance, chewing, mood and anxiety and deterioration in regard to swallowing. Within-patient Kappa agreement between categories at 2 and 10 years was

generally fair to moderate, with slightly more agreement observed for physical function domains than for social-emotional domains (Table 4). The standard deviations for individual change scores indicate considerable scatter between two year and ten-year scores (Table 5).

In regard to overall QOL being less than good the agreement between 2 and 10 years was weak (kappa statistic of 0.21) and the increase observed overall (from 14%, 10/73 to 19%, 14/73) was not statistically significant (McNemar test, P=0.45). Median (IQR) physical function subscale scores were 74 (66-91) at 2 years and 78 (64-91) at 10 years, P=0.50 Wilcoxon paired test n=112; Median (IQR) social-emotional subscale scores were 83 (69-92) at 2 years and 83 (70-95) at 10 years, P=0.39 Wilcoxon paired test n=113.

DISCUSSION

There is a paucity of HRQOL data collected prospectively to 10 years following oral cancer. This is an important topic in respect to survivorship and late effects. Although our Unit has published outcomes research on both HRQOL [16] and survival following oral cancer [17] longitudinal changes up to 10 years have not been reported before. Our longitudinal design allows comment on changes from 2 years to 10 years and this study has the strength of being a relatively large sample of responders (154 patients) with 10 year HRQOL data with an acceptable response rate 67%. The study has limitations and one of these is that the UWQOL was not collected at fixed time points during follow-up but as part of 'annual' surveys. Hence the use of time windows to capture data close to certain time points. Secondly, in this aging patient population no attempt has been made to account for other comorbidities which might impact negatively on HRQOL. The sample is one of survivorship, with those dropping out probably reporting worse HRQOL. Lastly, it is inevitable that the cohort is historical, 1992 to 2004, and various new treatment strategies have emerged, such as Intensity-Modulated Radiation Therapy (IMRT) which could influence the long-term outcomes in more recently treated patients.

The sample does reflect survivorship in so much as there are relatively few patients aged 65 years and over at the time of treatment who are alive after 10 years and contributing UWQOL outcomes data, and especially so for those aged 75 years and over. Similarly, those with advanced stages of disease, having surgery and post-operative radiotherapy and those requiring composite free tissue transfer are relatively fewer at longer term follow-up than

when treated. This might partly explain the relatively good survival rate and relatively consistent reported quality of life characteristics between 2 and 10 years.

The long-term HRQOL outcomes we report appear relatively good across the domains of the UW-QOL in regard to dysfunction and high mean scores. Three-quarters stated their overall QOL to be good or better. It is possible that some domain scores might expect to fall naturally with age, such as activity, chewing, taste and saliva, but we could not explore this further as relevant normative data for the UW-QOL over time does not exist. [14]

It is very difficult to compare directly the findings of this current study with previous papers as each has different case mix characteristics. Yan et al [11] reported change in UW-QOL scores from 1 year to eight years in 30 oral cancer survivors. In this time period patients reported clinically significant improvements in appearance, recreation, speech, saliva and anxiety whilst the other seven items remained stable. In a cross-sectional survey using the UW-QOL in 26 patients 14.7 years (range, 3 to 27 years) following for oral cancer treated when they were 40 years of age or less, reported that 77% percent rated their overall QOL as outstanding, very good, or good.[10] Only radiotherapy seemed to adversely affect the overall QOL and the key domains affected were appearance, mood, saliva, and shoulder function. Long-term outcome with good to very good QOL was reported in 67 patients, two to ten years after preoperative chemoradiotherapy followed by surgery including microvascular reconstruction for advanced oral and oropharyngeal cancer. [6] In contrast a longitudinal assessment of 26 patients treated for advanced oral or oropharyngeal cancer with a mean of 9.2 years follow-up, (range 8-11 years), reported a number of HRQOL domains worsened significantly ($p < 0.01$) in the long-term: emotional functioning, social functioning, swallowing, speech, taste/smell, dry mouth, sticky saliva and coughing. [8] However. this was a group who were treated with free-flap reconstruction and postoperative radiotherapy and this could account for the deterioration. In an assessment of 22 patients at 10-years post-treatment after organ-preservation treatment, long-term functional voice and speech problems were common with fewer complaints in those treated with IMRT than with conventional radiotherapy [18] and also seen in swallowing and reduced mouth opening. [19]

When comparing across HRQOL at two years and at ten years in our sample it is notable that in this cohort of patients there is relatively little change at the group level. At most the mean changes were in the order of 4-6 units. According to Kazis et al [20] effect size can be obtained

by dividing mean change by the standard deviation (SD) in pre-change data, and a 'small' effect represents about 0.20 of SD, a 'moderate' effect about 0.50 of SD and a 'large' effect about 0.80 of SD. Our results at 1-2 years give domain SDs of around 20 and this would imply a 'small' mean change being equivalent to 4 units, a 'moderate' change of 10 units and a 'large' change of 16 units. Ringash et al [21] defined a minimal important difference as the smallest difference that reflects a clinically important change in score and stated that most published minimal important difference estimates fell into the range 5-10% of the instrument range, which for us would imply mean changes of about 5-10 units. Thus, it is reasonable to suggest that the changes we observed between mean scores at 2 and 10 years were small and just bordering on being clinically significant. There were improvements in appearance, chewing, mood and anxiety and deterioration in regard to swallowing. Although, as a cohort, HRQOL appears relatively stable after two-years, there is individual variation. The data shows considerable individual scatter in domain change scores (Table 5) and only fair to moderate agreement between 2 and 10 years regarding the 3 categories (Table 4, 'dysfunction', 'neither extreme' 'best possible'). It is hard to ignore that in Table 4 there was no Cohen's kappa score of greater than 0.60, the generally held criteria for defining good agreement, and hence that there was considerable within-patient instability between the results seen at 2 years and at 10 years.

CONCLUSION

In conclusion, in the long-term most patients following oral cancer report a good or better overall QOL. Those alive at 10 years were survivors, with survival linked to the baseline characteristics, as those more elderly and with advanced cancer were lost to follow-up. Group level changes between 2 and 10 years were small with some just bordering on being clinically significant with improvements suggested in appearance, chewing, mood and anxiety, with deterioration in swallowing. Individual patient level changes were not so stable.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interests.

AUTHORS CONTRIBUTIONS

Both authors conceived, designed, interpreted, reviewed and revised the manuscript. Detailed statistical analysis was performed by D Lowe (Medical Statistician).

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Table 1 Baseline characteristics and overall QOL for those alive at 10 years

Baseline characteristics		Alive at 10 years %	Alive at 10 years n/N	P value**	Overall QOL less than good* %	Overall QOL less than good* n/N	P value**	Median No. of months to UWQOL questionnaire
	TOTAL	34	230/674		26	39/151		121
Year	1992-1996	36	83/232		34	20/58		123
	1997-2001	35	94/269	0.53	24	16/67	0.08	121
	2002-2004	31	53/173		12	3/26		115
Gender	Male	32	137/426	0.18	25	24/95	0.84	121
	Female	38	93/248		27	15/56		122
Age	<55	50	86/172		32	19/60		123
	55-64	40	79/196	<0.001	21	12/58	0.39	121
	65-74	28	47/169		24	8/33		119
	75+	13	18/137					
Tumour site	Buccal	28	38/134		37	10/27		123
	Lower gum	32	24/76		25	3/12		120
	Tongue (ant 2/3)	44	87/200	0.02	20	11/56	0.08	120
	Floor of Mouth	32	69/215		20	9/45		121
	Other	24	12/49		55	6/11		123
Overall Clinical Stage	Early (0-2)	45	150/332	<0.001 excl	22	22/102	0.11	121
	Late (3-4)	24	80/339	NK	35	17/49		121
	NK		0/3					
Primary treatment	Surgery alone	45	166/367		25	27/107		122
	Surgery & RT	24	59/241	<0.001	29	12/42	0.83	121
	RT alone	8	5/66		0	0/2		108
Free-flap surgery	Yes - composite	27	45/169		45	13/29		123
	Yes - soft	38	103/271	0.001	26	20/77	0.01	122
	No flap	46	77/168		14	6/43		119
P stage (surgical cases)	Early (0-2)	51	131/258	<0.001 excl	20	18/88	0.06 excl	122
	Late (3-4)	28	93/333	NK	34	21/61	NK	121
	NK	6	1/17		0	0/2		105

NK: Not known

*151 of 230 alive at 10 years had overall QOL recorded from at least 8 years (96 months) on.

**Fishers exact test

Table 2. UWQOL domain results for154 OSCC patients alive at 10 years

		No.	Mean (SE) score	Dysfunction		Somewhere between		Best response	
UWQOL physical function subscale	Appearance	153	78.6 (1.6)	10%	16	53%	81	37%	56
	Swallowing	153	79.9 (2.2)	12%	19	34%	52	54%	82
	Chewing	151	71.9 (2.5)	7%	10	43%	65	50%	76
	Speech	153	81.1 (1.7)	7%	10	47%	72	46%	71
	Taste	152	74.6 (2.5)	9%	13	43%	65	49%	74
	Saliva	150	76.0 (2.3)	10%	15	44%	66	46%	69
UWQOL social-emotional function subscale	Pain	153	83.0 (1.8)	9%	14	37%	56	54%	83
	Activity	153	73.4 (2.0)	12%	19	50%	77	37%	57
	Recreation	153	77.6 (1.8)	7%	11	54%	82	39%	60
	Shoulder	152	78.1 (2.4)	13%	19	33%	50	55%	83
	Mood	154	80.5 (2.0)	12%	18	39%	60	49%	76
	Anxiety	152	82.0 (1.8)	9%	13	39%	59	53%	80

154 of 230 alive at 10 years had UWQOL data recorded from at least 8 years (96 months) on.

Table 3. UWQOL subscale scores and overall QOL at 10 years for OSCC patients

Physical function subscale score (0-100):		
<50	12%	19/153
50-69	21%	32/153
70-89	30%	46/153
90-100	37%	56/153
Median (IQR) score	80 (65-95), N=153	
Social-emotional function subscale score (0-100):		
<50	9%	14/154
50-69	16%	24/154
70-89	40%	61/154
90-100	36%	55/154
Median (IQR) score	83 (70-95), N=153	
Overall QOL:		
Very poor / Poor	7%	10/151
Fair	19%	29/151
Good	36%	54/151
Very good/Outstanding	38%	58/151
Good or better	74%	112/151

154 of 230 alive at 10 years had UWQOL data recorded from at least 8 years (96 months) on.
Subscale scores were computed so long as there were 4 or more domain scores available.

Table 4. UWQOL Dysfunction at 2 and 10 years

			TWO years						TEN years						Change	Kappa coefficient of agreement (SE) between the 3 categories over time
		No. with 2 and 10 years	Dysfunction		Somewhere between		Best response		Dysfunction		Somewhere between		Best response		P value*	
UWQOL physical function subscale	Appearance	101	10%	10	60%	61	30%	30	8%	8	54%	55	38%	38	0.08	0.32 (0.08)
	Swallowing	112	5%	6	39%	44	55%	62	13%	15	33%	37	54%	60	0.03	0.43 (0.07)
	Chewing	111	6%	7	55%	61	39%	43	5%	6	47%	52	48%	53	0.12	0.42 (0.08)
	Speech	112	3%	3	61%	68	37%	41	6%	7	52%	58	42%	47	0.18	0.55 (0.07)
	Taste	77	9%	7	36%	28	55%	42	6%	5	43%	33	51%	39	0.38	0.54 (0.09)
	Saliva	73	14%	10	41%	30	45%	33	11%	8	44%	32	45%	33	0.21	0.59 (0.08)
UWQOL social-emotional subscale	Pain	107	8%	9	33%	35	59%	63	8%	9	34%	36	58%	62	>0.99	0.50 (0.08)
	Activity	100	4%	4	52%	52	44%	44	9%	9	48%	48	43%	43	0.19	0.19 (0.09)
	Recreation	107	8%	9	50%	54	41%	44	5%	5	52%	56	43%	46	0.62	0.43 (0.08)
	Shoulder	107	11%	12	22%	24	66%	71	10%	11	31%	33	59%	63	0.50	0.22 (0.08)
	Mood	74	11%	8	45%	33	45%	33	4%	3	42%	31	54%	40	0.02	0.36 (0.09)
	Anxiety	73	12%	9	40%	29	48%	35	5%	4	40%	29	55%	40	0.27	0.35 (0.09)

*McNemar-Bowker test

Table 5. UWQOL mean domain scores at 2 and 10 years

		No. with 2 and 10 years	TWO years Mean (SE)	TEN years Mean (SE)	CHANGE Mean (SD)	95% CI: mean change	P value*
UWQOL physical function subscale	Appearance	112	74.3 (1.9)	78.8 (1.8)	4.5 (21.5)	0.4, 8.5	0.03
	Swallowing	112	84.2 (1.9)	79.9 (2.5)	-4.3 (25.0)	-9.0, 0.4	0.07
	Chewing	111	66.2 (2.8)	71.2 (2.8)	5.0 (29.3)	-0.6, 10.5	0.08
	Speech	112	79.9 (1.6)	80.1 (1.8)	0.2 (17.3)	-3.1, 3.4	0.91
	Taste	77	80.4 (3.0)	76.9 (3.3)	-3.5 (22.7)	-8.7, 1.6	0.18
	Saliva	74	74.2 (3.4)	74.3 (3.5)	0.1 (24.6)	-5.6, 5.8	0.96
UWQOL social-emotional subscale	Pain	113	83.2 (2.1)	82.5 (2.2)	-0.7 (18.8)	-4.2, 2.8	0.71
	Activity	112	77.5 (2.1)	75.5 (2.3)	-2.0 (24.7)	-6.6, 2.6	0.39
	Recreation	113	78.5 (2.1)	79.6 (2.0)	1.1 (21.2)	-2.9, 5.1	0.58
	Shoulder	110	81.3 (2.9)	80.5 (2.6)	-0.8 (27.8)	-6.1, 4.4	0.76
	Mood	74	79.0 (2.9)	85.1 (2.3)	6.1 (25.8)	0.1, 12.1	0.05
	Anxiety	74	79.0 (2.9)	84.2 (2.3)	5.2 (24.6)	-0.5, 10.9	0.08

*paired t-test